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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,869	05/04/2001	David J. Anderson	CALTE.004C1	1088

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,869	ANDERSON ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-86* is/are pending in the application.

4a) Of the above claim(s) *1-56,62-65 and 84-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-61 and 66-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1) Claims 1 to 86 are pending in the instant application.

2) As indicated by Applicant in the correspondence of 23 October of 2003, the previous office action was inadvertently directed to a non-elected invention. Therefore, that office action is hereby vacated and a substitute office action directed to the elected invention follows.

3) Claims 1 to 56, 62 to 65 and 84 to 86, As well as claims 57 to 61 and 66 to 83 in so far as they relate to any of the sequences recited therein other than SEQ ID NO:16, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 23, filed 09 June of 2003.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4) Claims 57 to 61 and 66 to 83 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. These claims are drawn to a method of identifying ligands, agonists and antagonists of a "Mrg polypeptide", and specifically a "Mrg X" polypeptide comprising the amino acid sequence presented in SEQ ID NO:16 of the instant application. The instant application has provided a description of an isolated DNA encoding a protein identified therein as a "Mrg X" protein, and the protein encoded thereby. Whereas the instant specification discloses that the elected Mrg X protein is a human G protein-coupled receptor that is expressed in the dorsal root ganglia (DRG), it does not disclose a **specific** biological role for this protein or its significance to a particular disease,

disorder of physiological process which one would wish to manipulate for a desired clinical effect by administering a compound that has been identified by the claimed method. The instant specification describes a plurality of proteins, many of which are members of the G protein-coupled receptor family, and identified therein as "Mrg polypeptides", that appear to be expressed almost exclusively in dorsal root ganglia. The instant specification further discloses that dorsal root ganglia is involved in nociception. However, the instant specification does not ascribe a specific role for the elected Mrg X protein in nociception and one of ordinary skill would not reasonably believe that all of the plurality of different putative DRG-associated receptor proteins described in the instant specification play a common role in nociception. Further, because the instant specification does not credibly identify, with specificity, the effects that the administration of a "Mrg X" agonist or antagonist which has been identified by the claim method is going to have on an organism when administered thereto, the identification of such agonists and antagonists is of no immediate practical value in currently available form.

It is clear from the instant specification that the receptor proteins identified therein as "Mrg X" are what are termed an "orphan receptors" in the art. An orphan receptor is a protein whose cDNA has been isolated because of its similarity to known receptor proteins. There is little doubt that, after complete characterization, the elected protein and agonists and antagonists thereto may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete.

Whereas one could readily employ a putative receptor protein of the instant invention in the claimed assay to identify ligands thereto the information obtained thereby would be of little use until one discovers the identity of those physiological processes moderated by that putative receptor. Because the instant specification has failed to credibly identify a physiological process **which has been shown** to be influenced by the activation or inhibition of a putative receptor protein of the instant invention an artisan would have no way of predicting what effects the administration of that ligand to an organism would have. The assertion that the elected Mrg X protein is involved in pain sensation or transmission is of little value unless one knows specifically what effects the activation or inhibition of that protein is going to have on a subject. If one can not predict the effects that the administration of a ligand of the putative receptor of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that ligand.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. ' 101, which requires that an

invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a process of identifying agonists and antagonists of a protein of as yet undetermined function or biological significance. There is no evidence of record or credible line of reasoning that would support a conclusion that a protein of the instant invention is associated in any way with the plurality of disorders that are listed on page 29 of the instant specification. Until some actual and specific significance can be attributed to any one of the plurality of proteins identified in the specification as Mrg X proteins, or the genes encoding them, the instant invention is incomplete. The protein employed in an assay of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as G protein-coupled receptors. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible and practical "real world" use for the elected Mrg X protein in its currently available form then the claimed assay is

incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5) Claims 57 to 61 and 66 to 83 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

6) Claims 75 to 81 and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and the enablement requirements. These claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to an assay that requires a "known Mrg polypeptide agonist". Whereas claim 83 does not expressly require this element, the only functional definition of a "neutralizing antibody" provide on page 27 of the instant specification requires the antibody to inhibit or reduce activation of a particular receptor "by a known ligand". A ligand that activates a receptor is defined in the art as an agonist for that receptor. The instant specification does not enable one to practice the method as claimed because it does not adequately describe a known agonist for a polypeptide comprising the amino

acid sequence presented in SEQ ID NO:16 of the instant application. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [t]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

Because the instant specification does not describe the required agonist by such descriptive means "as words, structures, figures, diagrams, formulas, etc., that set forth the" the required agonistic compound it not only fails to provide all of the critical information needed to practice the claimed assay, it also fails to describe that critical element in terms that are sufficient to show that Applicant was actually in possession of that critical element at the time that the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7) Claims 57 to 61 and 66 to 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. These claims are vague and indefinite in so far as they employ the term "Mrg polypeptide" as a limitation. Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "Mrg polypeptide" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. The text on pages 18 and 19 of the instant application describe "Mrg" as a "Mas related gene". It is noted that the *Mas* oncogene is a member of the G protein-coupled receptor family, all of whose members are structurally and functionally "related" to some extent. Because the instant specification does not explain how a "Mas related" G protein-coupled receptor is structurally distinct from other members of the G protein-coupled receptor family, one can not determine if any particular member of the G protein-coupled receptor family is "Mas related" or not and, therefore, one can not determine if that protein is encompassed or excluded by the limitation "Mrg polypeptide".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the

previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

8) Claims 57 to 61, 66 to 74 and 82 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Ahmad et al. patent publication (WO 99/32519, cited by Applicant), which provided a written description of the claimed assay on pages 3 to 5, 13 and 14 therein. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above and it is a divisional of application Serial Number 09/704,707, the prior application also does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120.

9) Applicant's arguments with respect to claim 16 have been considered but are moot in view of the new ground(s) of rejection. The argument that a polypeptide of the instant invention has specific and substantial utility as a tissue marker is irrelevant to claims that are drawn to an assay for the identification of agonists or antagonists of that polypeptide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1600